REMARKS

A. Applicants that the Examiner for the helpful interview conducted on August 26, 2003. Applicants' Statement of Substance of Interview is enclosed herewith.

B. Claims 3 and 5 are all the claims pending in the application; both of the claims have been rejected.

Claims 3 and 5 have been amended to more clearly recited that which Applicants regard as their invention. Support for recitation of "cross-linking" agent in place of "hardening" agent is inherent given the compounds that may be used for this purpose listed at page 10, lines 18-32, of the specification.

Recitation of "dried" thin membranes may be found in the Examples of the specification, for example, in Example 1, page 15, lines 24-27.

Entry of the amendment is respectfully requested. No new matter has been added.

I. Rejection Under 35 U.S.C. §102

At the bottom of page 2 of the Office Action, claim 3 is rejected under 35 U.S.C. §102(b) as being anticipated by Galis et al. (1995).

The Examiner states that Galis et al. teaches a method of detecting a protease in a biological sample wherein consecutive sections of the sample are brought into contact with a thin membrane comprising a support holding a fluorescent substrate mixed with agarose, and other sections are brought into contact with similar thin membranes with protease inhibitors incorporated, and the results from the two are compared. The Examiner further states that Galis et al. teaches use of an agarose to stabilize the substrate film. The Examiner asserts that because agarose is well-known to be "hard" at room temperature, it is a "hardening agent" and claim 3 is anticipated.

In response, Applicants note that the "hardening" agent recited in the claims as filed is used to form "cross-linking" of the substrate proteins to form the thin membrane. This action of the hardening agent to form cross-linkages will be readily understood by the skilled artisan by reference to the specific compounds exemplified as "hardening agents" at page 10, line 12-32, of the specification.

In contrast, while agarose used in the thin membrane of Galis et al. may be "hard" at room temperature as suggested by the Examiner, it does not form cross-linkages between the proteins comprising the thin membrane. Accordingly, agarose would not fall within the scope of the hardening agents of the present invention.

For the sake of clarity, Applicants include herewith an amendment to the claims wherein "cross-linking" agents are recited in place of "hardening" agents.

As Galis et al. does not teach a cross-linking agent, Galis et al. does not anticipate the claims as amended. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

II. Rejection Under 35 U.S.C. §103

At the top of page 4 of the Office Action, claims 3 and 5 are rejected under 35 U.S.C. §103(a) as being unpatentable over Galis et al. (1995) in view of Terashima et al. (USP 4,839,278, issued June 13, 1989) and Lawrence et al. (USP 5,416,003, issued March 16, 1995).

The Examiner states that Galis et al. teaches a method of detecting a protease as described above, but that it does not teach a multiply layered thin film as recited in claim 5.

The Examiner goes on to state that Lawrence et al. teaches a device for detecting proteases in samples wherein multiple layers are laminated together, and wherein one layer may

comprise a substrate and another layer may comprise an inhibitor. The Examiner further states that Terashima et al. teaches a variety of reagents for cross-linking (hardening) gelatin on a thin film, and teaches that these are similar in function to agarose.

The Examiner concludes that it would have been obvious to have laminated a layer comprising a substrate, hardener and inhibitor to a layer comprising a substrate and a hardener in a multilayer analytical element. The Examiner asserts that the motivation would have been to facilitate measurement of proteases in a single sample using a single test element.

In response, Applicants first refer to their comments above regarding the amendment of the claims to recite a "cross-linking" agent and the failure of Galis et al. to teach a cross-linking agent. Indeed, the system disclosed in Galis et al. is prepared by simply adding agarose to gelatin, which means that the structure of the gelatin (the protease substrate taught in Galis et al.) is not chemically altered and that no alteration of the physical properties of the gelatin is achieved by mixing agarose with the gelatin.

In contrast, according to the present invention, the use of a cross-linking agent gives rise to the formation of covalent bonds between molecules of gelatin to thereby alter the chemical structure of the gelatin. As a result, an optimum sensitivity of the membrane to a protease is achieved. In Table 3 of the specification (page 26), the results of Sample 107 and Samples 116 to 118 demonstrate the effects of amounts of cross-linking agents on the properties of the membranes. From these experimental results, one of ordinary skill in the art would easily recognize that the cross-linking in the claimed thin membrane can achieve superior sensitivities of the thin membrane to a protease.

In addition, Galis et al. discloses only the use of wet membrane, while in contrast, the thin membrane of the instant application is used in a dried state. The dried thin membrane of the

present invention has superior properties such as high storage stability and reduced fluctuations in experimental values. The claims as amended herein recite the use of a dried thin membrane in all embodiments.

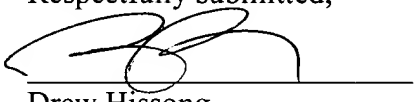
As the prior art neither teaches nor suggests the use of a cross-linking agent to achieve the superior sensitivities of the thin membranes, nor the use of a dried thin membrane to achieve high storage stability and reduced fluctuations in experimental values, Applicants respectfully assert that none of the cited art, either alone or in combination, teaches or suggests the instantly claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

II. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Drew Hissong
Registration No. 44,765

Date: October 20, 2003